Remarks

Applicants have amended claim 1 to a preferred embodiment, namely, to a pharmaceutical composition comprising anakinra and IL-18 binding protein. Support for the amendment can be found throughout the specification and original claim, for example, claim 33, and page 2, lines 13-14. Applicants have further amended claim 31 to specifically claim that the therapeutically effective amount of anakinra is an amount that results in inhibition of IL-1 activity, and that the therapeutically effective amount of IL-18BP is an amount that results in inhibition of IL-18 activity. Support for these amendments can be found, for example, at page 24, lines 11-19. Accordingly, no new matter has been introduced by the amendments and their entry is respectfully requested. Applicants have cancelled claims 32-36 to comply with the amendment. Claims 37-67 have been cancelled as directed to non-elected inventions. Applicants reserve the right to pursue claims to subject matter of any of these claims or other cancelled subject matter in any continuation applications.

Applicants now turn to the specific objections and rejections.

The Examiner objected to the title for allegedly not being descriptive. Applicants respectfully submit that the new title obviates the objection.

Applicants respectfully submit that the Examiner's objections to claims 34-36 have been rendered moot in view of cancellation of these claims. Applicants further submit that the amendment to claim 31 has rendered the Examiner's objection to also claim 31 moot.

The Examiner rejected claims 31-36 as allegedly not complying with 35 U.S.C. §112, second paragraph, definiteness rejection. Specifically, the Examiner alleged that the term "therapeutically effective amount" is indefinite because it does not refer to a disease or condition. The Examiner further contended that the term "antagonist/inhibitor of IL-1" is not defined.

Applicants have amended claim 31 as described, *supra*. Accordingly, Applicants respectfully submit that claim 31 now fully complies with 35 U.S.C. §112, second paragraph definiteness requirement.

Claims 32-36 have been cancelled and therefore the rejections regarding these claims have been rendered moot.

In view of the above, Applicants respectfully submit that the rejection of claim 31 35 U.S.C. §112, second paragraph, should be withdrawn.

The Examiner rejected claims 31-33 as allegedly not complying with 35 U.S.C. §112, first paragraph written description requirement. Specifically, the Examiner alleged that the terms "mutein, functional derivative, fractions, circularly permutated derivative, fused protein, isoform and salt thereof" of IL-18BP are not sufficiently defined.

While Applicants respectfully disagree, Applicants have amended claim 31 as described, *supra*. In view of the amendment and the cancellation of claims 32-33, Applicants submit that the rejection has been rendered moot.

The Examiner rejected claims 31 and 34-36 under 35 U.S.C. §102(b) as allegedly anticipated over a U.S. patent application publication No. 2002/0098185 to Sims et al. ("Sims").

Applicants respectfully submit that the rejection should be withdrawn for the following reasons.

Claim 31 has been amended to a specific combination of anakinra and IL-18BP. As acknowledged by the Examiner on page 6 of the October 21, 2009 Office Action, "Sims does not specifically mention that the IL-1 antagonist is IL-1Ra or Kineret." KINERET® is a registered trademark for marketing anakinra. Accordingly, Sims does not disclose all the elements of the amended claim 31, and the rejection should be withdrawn. Claims 34-36 have been cancelled and the rejections have thus been rendered moot.

The Examiner rejected claims 32 and 33 under 35 U.S.C. §103(a) as allegedly obvious over Sims in view of U.S. Patent No. 7,005,523 to Dombroski et al. ("Dombroski").

Applicants respectfully disagree and submit that the rejection be withdrawn for the following reasons.

The claims are directed to a composition with a specific combination of anakinra and IL-18BP.

While a general combination of IL-18 antagonists in general with IL-1 antagonists in general is described in Sims (par. [0051]), there is no teaching or suggestion to a person of ordinary skill in the art having common sense at the time the invention was made of the specific combination of IL-18BP and anakinra. The list of possible combinations in Sims includes not only IL-1 antagonists but also antagonists to IFNγ, IL-6, IL-8, IL-12, IL-15 and TNF, particularly TNFα (see par. [0052]). Dombroski describes numerous possible combinations of TNFα inhibitor with other molecules, including a soluble IL-1ra, e.g., Kineret, but also lists COX-2 inhibitors, metalloproteinase inhibitors, p2X7 inhibitors, α2δ inhibitors, low dose

metotrexate, leflunomide, hydroxychloroquine, d-penisillamine, auranofin, or gold as possible combination treatments with TNFα, and tens, if not hundreds of additional agents are listed in the specification (col. 15, lines 32-67, and col. 16, lines 1-17). Based on these extensive lists of compounds in both Sims and Dombroski, resulting in tens of thousands of possible combinations, a person of ordinary skill in the art would have required extensive experimentation to arrive to the specific claimed combination of anakinra and IL-18BP. There is no specific guidance or reasoning to allow a skilled artisan to pick any of the combinations for treating any disease based on the combination of Sims and Dombroski.

Only when pointed out in the present application using non-permitted hindsight, a skilled artisan would have learned of the particular usefulness of the combination of anakinra and IL-18BP. As described in the specification, Applicants unexpectedly found that IL-1 is essential for induction of IL-18BP by interferon gamma (see par. [0041]). This finding led to the discovery that there is a specific need to supplement IL-18BP in patients who receive medication inhibiting IL-1 to avoid the side effect of increased risk of viral infections known to be a significant side effect of Kineret monotherapy (Id., and Exhibit I). In fact, as specifically indicated in Exhibit I, a product information sheet for Kineret from the manufacturer, a skilled artisan would have been specifically taught away from using a combination of other inhibitors, listed in both Sims and Dombroski, such as TNF blocking agents with Kineret.

Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §103(a) Sims in view of Dombroski is improper and should be withdrawn.

In view of the foregoing, Applicants respectfully submit that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the Commissioner is hereby is authorized to charge our deposit account No. 50-0850. Any overpayments should also be deposited to said account.

Date: March 3, 2009

Respectfully submitted,

/Leena H. Karttunen/

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